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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/814,338	03/21/2001	Jonathan M. Rothberg	21465-501 CIP2	6233

35437 7590 06/28/2006

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EXAMINER

KIM, YOUNG J

ART UNIT PAPER NUMBER

1637

DATE MAILED: 06/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No. 09/814,338	Applicant(s) ROTHBERG ET AL.	
	Examiner Young J. Kim	Art Unit 1637	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 30 May 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 5 months from the mailing date of the final rejection.
 b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
 (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
 (b) ☐ They raise the issue of new matter (see NOTE below);
 (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
 (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

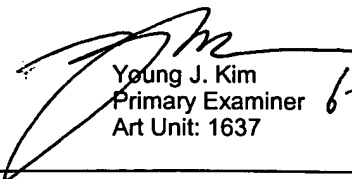
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
 5. ☐ Applicant's reply has overcome the following rejection(s): _____.
 6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
 7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
 The status of the claim(s) is (or will be) as follows:
 Claim(s) allowed: _____.
 Claim(s) objected to: _____.
 Claim(s) rejected: _____.
 Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☒ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
 9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
 10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See Continuation Sheet.
 12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____.
 13. ☐ Other: _____.


 Young J. Kim
 Primary Examiner
 Art Unit: 1637

Continuation of 11. does NOT place the application in condition for allowance because: Preliminarily, the evidence submitted as exhibits, submitted with the after final amendment received on May 30, 2006 are not the same as those which were presented during prosecution. Applicants do not point out as to why these evidences of record were not earlier presented, and as such, the submission is improper and non-considered. The present response will address Applicants' arguments to the extent possible in view of the earlier evidence submitted before the Office. Applicants, on page 2 of the Response, contend that the obviousness rejection maintained in the Final Office Action mailed on December 29, 2005 had not: 1) consider and address the evidence of the unexpected results and long-felt need for the claimed invention; 2) properly evaluate the objective evidence as rebuttal to an alleged prima facie case; and 3) evaluate the nexus of the objective evidence to the claimed invention.

1) Office requirement to fully consider and address Applicants' arguments:

Applicants assert that in their Response filed on October 14, 2005, provided evidence of proof of unexpected results; long-felt need and 3) commercial success and that the Office Action did not properly consider and address the above. It will be demonstrated herein that the Office Action mailed on December 29, 2005 did address all of the issues that Applicants' had raised. It is also stated herein that Applicants' response filed on October 14, 2005 only relied on the unexpected results; long-felt need and commercial success of the claimed invention.

Applicants have pointed to a plurality of publications (Nature, New York Times, and 454 Press Release) which discusses the capability of the claimed system to sequence nucleic acid sequences expediently with accuracy (Nature article); making a giant strides toward the goal of sequencing human genome cheaply (New York Times); producing more than 20 million bases per sequencing run, which is 100 times the capacity of other sequencing systems (454 Press Release) (see page 3, Response).

However, What Applicants have failed to point out was whether these attributes of the claimed invention are a direct result of having a fiber optic "wafer." It should be pointed out that the Office Action which was made Final was based on the "fact" that Chee et al. (of record) already disclosed a fiber optics array which comprised all of the claimed limitation, "except" that the array was not in a wafer format (having a depth of instantly claimed range). The obviousness rejection was made in view of Krull et al. (also of record) that the depth of the fiber optic wafer (1 cm) is optically coupled to a bundle of fiber optics for detection (see pages 3-5 of the Office Action). In that Office Action, it was clearly stated that the invention produced by the combination of Chee et al. would have produced the same results since Chee et al. already disclosed the same array with the only exception that the array did not have the depth limitation (i.e., wafer format). And since Applicants did not clearly convince (by evidence) that the reason for the commercial success, the efficiency of the sequencing reaction all resulted from the fact that the claimed array was in a "wafer" format, the rejection was maintained (see pages 9-10 of the Final Office Action).

Contrary to Applicants' assertion that Examiner dismissed the commercial evidence of nonobviousness is simply not true. On pages 9 and 10 of the Office Action, the following was stated:

"While Applicants provide evidence which demonstrate that the claimed invention might be commercially successful, Applicants have failed to demonstrate which aspect of the claimed invention is responsible for the asserted success (or providing a nexus between the commercial success and the of the claimed invention). The prima facie showing of obviousness was based on the fact that the method of pyrosequencing via use of the substrate disclosed by Chee et al. met all of the limitation of the claimed invention except that the substrate did not have a "wafer" configuration. However, the prima facie showing was made that even Applicants' substrate, for it to work, had to be coupled to a matching set of long fused fiber optic bundles so as to couple to the imaging device, the resulting working apparatus of which would be identical to that of Chee et al. Applicants have failed to demonstrate just which aspect of the instant invention that is different from that of Chee et al. is responsible for the commercial success. As the sole difference between the invention of Chee et al. and that of the claimed invention is in the wafer configuration, it is asserted that the method produced by the combination of Chee et al. and the Krull et al. would also be able to perform highly efficient sequencing reaction, absent evidence to the contrary." (Final Office Action, pages 9-10).

Clearly, the Office Action addressed why the evidences submitted by Applicants did not sufficiently overcome the prima facie showing of obviousness.

While Applicants contend that even if every element of the claimed invention is taught or suggested in the cited reference, the claimed invention can still be considered nonobvious with sufficient showing of unexpected results, long-felt need, and commercial success. (page 5, 2nd paragraph, Response).

While in certain situations the above arguments would be valid, it certainly is not valid in the instant application.

Applicants appear to be contending that the asserted "unexpected results" or the "commercial success" directly resulted from the "wafer" format of the array. Consider an example when prior art discloses an array having a 10 cm depth. Now consider an application which contains the same material of the prior art array, except that the depth of the application is limited to 2-3 cm. The application does not disclose any unexpected results based on its depth nor do Applicants present any evidence which shows that the commercial success is directly tied to the depth of the array. Clearly, the claimed array would be obvious over the array of the prior art. Simply put, the showing of commercial success, or the unexpected results must be tied to the invention which is held to be non-obvious over the prior art, which, in the instant situation, is the wafer configuration of the claimed array. None of Applicants' evidence show that the commercial success, unexpected results were produced from the fact that the array was in a wafer format.

On page 6 of the Response, Applicants attempt to show "unexpected results" of the instant application. However, Applicants failed to evidence whether the fiber optic array of Chee et al. cannot achieve the same result, nor do the Applicants show that such result is produced from the "wafer" format. These arguments are clearly not found persuasive.

With regard to Applicants' arguments drawn to a long-felt need, these arguments are not found persuasive because Chee et al. already disclose a fiber optical array which pyrosequences nucleic acids. Applicants are not the first to pyrosequence nucleic acid sequences on a fiber optic array. Chee et al. are. The long-felt need to improve upon traditional sequencing methods such as Sanger dideoxy termination sequencing, was also recognized by Chee et al.

Applicants attempt to establish a nexus between the claimed invention with that of the commercial success (page 12, Response).

a) a fiber diameter of 47 um.

Applicants are advised that the pending claims do not recite this diameter, but rather a large range of diameters 6-50 um.

Chee et al. further contemplate such diameters (see section [0117], wherein the beads in the cavitated surface of the array comprises a diameters of 0.2 to 200 microns (or um).

b) fiber optic slide etched to produce 1.6 millions wells.

Applicants are advised that the claims do not recite this limitation.

Chee et al. further contemplates an array which detects 1, 2, 5, and 10 million probe arrays (see section [0104]).

c) well depth of 55 um.

The well depth is not recited in the pending claims.

As shown by Figure 1, the optical fibers of Chee et al. are etched (cavitated). It is asserted that the depth is within the claimed range absent evidence to the contrary.

d) beads attached to genomic DNA.

As shows by Figure 1 of Chee et al., the beads comprise DNA.

e) beads attached with sulfurylase and luciferase as sequencing enzymes.

Not all claims have this recitation, but rather a generic limitation "pyrosequencing reagents."

Chee et al. already disclose these embodiments (see section [0040]).

f) a flow chamber for holding the fiber optic slide.

g) fluidic assembly for delivering individual nucleotides - Chee et al. discloses chambers for accepting and washing nucleotides.

In addition, it is not found convincing that the presence of a flow chamber of fluidic assembly is what resulted in the commercial success.

Applicants appear to be simply reciting the limitations which are either not present in the claims or simply recited in the claims without any explanation as to how each of these elements resulted in the commercial success.

Applicants' reiteration of the teachings of Krull reference and its combination are also not found convincing since Applicants are discussing the teachings of the prior art separately.

Applicants are encouraged to file an Appeal Brief for the matters surrounding the patentability of the instant application.